

# WEST Search History

DATE: Wednesday, April 09, 2003

<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
side by side			
	<i>DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR</i>		
L5	(sublingual or buccal) and L2	16	L5
L4	(sublingual or buccal) and L3	0	L4
L3	L2 same testosterone same ester	53	L3
L2	androgen same mixture	281	L2
L1	androgen same mixture testosterone same ester	972	L1

END OF SEARCH HISTORY

=> d his full

(FILE 'HOME' ENTERED AT 17:05:29 ON 07 APR 2003)

FILE 'CAPLUS, MEDLINE' ENTERED AT 17:06:21 ON 07 APR 2003

L1 0 SEA ABB=ON PLU=ON TESTOSTERONE (P) ET SER (3A) (ACETATE OR UNDECANOATE OR PROPIONATE OR DECANOATE OR ENANTHATE)

L2 0 SEA ABB=ON PLU=ON TESTOSTERONE (P) ET SER (P) (ACETATE OR UNDECANOATE OR PROPIONATE OR DECANOATE OR ENANTHATE)

L3 546 SEA ABB=ON PLU=ON TESTOSTERONE (P) ESTER (P) (ACETATE OR UNDECANOATE OR PROPIONATE OR DECANOATE OR ENANTHATE)

L4 100 SEA ABB=ON PLU=ON TESTOSTERONE (P) TESTOSTERONE (3A) ESTER (5A) (ACETATE OR UNDECANOATE OR PROPIONATE OR DECANOATE OR ENANTHATE)

L5 13 SEA ABB=ON PLU=ON TESTOSTERONE (P) TESTOSTERONE (3A) ESTER (5A) (ACETATE OR UNDECANOATE OR PROPIONATE OR DECANOATE OR ENANTHATE) (P) (COMBINATION OR COMBINED)

L6 0 SEA ABB=ON PLU=ON L5 AND (BUCCAL OR BUCCALLY) (P) (ADMINISTER ED OIR ADMINISTRATION)

L7 0 SEA ABB=ON PLU=ON L5 AND (BUCCAL OR BUCCALLY) (P) (ADMINISTER ED OR ADMINISTRATION)

L8 0 SEA ABB=ON PLU=ON L5 AND (BUCCAL OR BUCCALLY)

L9 9 DUP REM L5 (4 DUPLICATES REMOVED)  
D L9 IBIB KWIC 1-

L10 2 SEA ABB=ON PLU=ON L4 AND BUCCAL

L11 2 DUP REM L10 (0 DUPLICATES REMOVED)  
D L11 IBIB KWIC 1-

L12 10 SEA ABB=ON PLU=ON TESTOSTERONE (P) BUCCAL (3A) ADMINISTRATION

L13 3 SEA ABB=ON PLU=ON L12 AND BIOADHESIVE

L14 2 DUP REM L13 (1 DUPLICATE REMOVED)  
D L14 IBIB KWIC 1-

L15 7 DUP REM L12 (3 DUPLICATES REMOVED)  
D L15 IBIB KWIC 1-

L16 0 SEA ABB=ON PLU=ON L15 AND SPRAY DRY?

L17 0 SEA ABB=ON PLU=ON TESTOSTERONE AND BUCCAL AND SPRAY (3A)  
DRY?

L18 3 SEA ABB=ON PLU=ON TESTOSTERONE (P) SPRAY (3A) DRY?

L19 1 SEA ABB=ON PLU=ON BUCCAL (P) BIOADHESIVE AND (SPRAY-DRYING OR SPRAY (2A) DRIED)  
D L19 IBIB KWIC 1-

L20 12 SEA ABB=ON PLU=ON BUCCAL (P) (SPRAY-DRYING OR SPRAY (2A)  
DRIED)

L21 10 SEA ABB=ON PLU=ON BUCCAL (P) (SPRAY-DRYING OR SPRAY (2A)  
DRIED) (P) TABLET

L22 1 SEA ABB=ON PLU=ON (L20 OR L21) AND TESTOSTERONE  
D L22 IBIB KWIC

L23 0 SEA ABB=ON PLU=ON BUCCAL (P) TABLET AND TESTOSTERONE

L24 27 SEA ABB=ON PLU=ON BUCCAL (P) TABLET AND TESTOSTERONE

L25 6 SEA ABB=ON PLU=ON L24 AND TESTOSTERONE (P) ESTER

L26 21 DUP REM L24 (6 DUPLICATES REMOVED)

L27 4 DUP REM L25 (2 DUPLICATES REMOVED)  
D L27 IBIB KWIC 1-  
D L21 IBIB KWIC 1-

L15 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS

DUPPLICATE 2

ACCESSION NUMBER: 1996:8351 CAPLUS

DOCUMENT NUMBER: 124:76746

TITLE: Pharmacokinetics of a single dose of Buccal testosterone

AUTHOR(S): Kim, Seokjoong; Snipes, Wallace; Hodgen, Gary D.; Anderson, Freedolph

CORPORATE SOURCE: Jones Institute Reproductive Medicine, Eastern Virginia Medical School, Norfolk, VA, 23507, USA

SOURCE: Contraception (1995), 52(5), 313-16  
CODEN: CCPTAY; ISSN: 0010-7824

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The bioavailability, pharmacokinetics, and metab. of a novel transbuccal delivery system of **testosterone** was investigated in five healthy eugonadal men. Total serum **testosterone** (T), dihydrotestosterone (DHT), and sex hormone-binding globulin (SHBG) concns. were detd. from blood samples obtained at 8:00 a.m. (zero hour), and 30 min and 1, 2, 3, 4, 6, 12 and 24 h later on day 1, and again on day 2, after dosing. This single transbuccal **administration** of **Buccal** T induced a prompt rise in serum T and DHT concns. The maximal concn. (Cmax) of T was 19.56 7.64 ng/mL (mean; 5.3-fold increase from the baseline) at 30 min (Tmax) after administration. The elimination half-life of Buccal T was about 1.75 h. Serum DHT peaked at 1 h at a concn. of 1.46 ng/mL (2.3-fold increase from the baseline). The drug was well tolerated. This study suggests that the Buccal T is a promising delivery system for natural T.

L15 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS

DUPPLICATE 3

ACCESSION NUMBER: 1986:193013 CAPLUS

DOCUMENT NUMBER: 104:193013

TITLE: Hydrophilic cyclodextrin derivatives enable effective oral administration of steroid hormones

AUTHOR(S): Pitha, Josef; Harman, S. Mitchell; Michel, Mary Ellen

CORPORATE SOURCE: Natl. Inst. Aging, Baltimore, MD, 21224, USA

SOURCE: Journal of Pharmaceutical Sciences (1986), 75(2), 165-7

CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Condensation products of .beta.-cyclodextrin with propylene oxide or epichlorohydrin, which are amorphous and thus very sol. in water, were used to form complexes with **testosterone** [58-22-0], progesterone [57-83-0], and estradiol [50-28-2]. Sublingual/**buccal administration** of tablets of these complexes led to effective absorption and entry of the hormones into the systemic circulation, followed by gradual elimination; rapid first-pass loss was avoided. .beta.-Cyclodextrin itself, its 2,6-di-Me deriv., and a nonionic detergent did not enable effective buccal absorption. Absorption from the GI tract of hormones complexed with hydrophilic cyclodextrins was also less effective. Effective absorption of drugs from the oral cavity requires that the drug and solubilizer form a complex of the inclusion type which dissolves completely and rapidly and that the solubilizer neither enters nor damages oral tissue.

L26 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1991:614845 CAPLUS  
DOCUMENT NUMBER: 115:214845  
TITLE: Low-melting moldable pharmaceutical excipient and dosage forms prepared therewith  
INVENTOR(S): Snipes, Wallace C.  
PATENT ASSIGNEE(S): Zetachron, Inc., USA  
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 257,569.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5004601	A	19910402	US 1988-264747	19881031
US 5135752	A	19920804	US 1988-257569	19881014
EP 390911	A1	19901010	EP 1989-911956	19891012
EP 390911	B1	19950301		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE			
JP 03501737	T2	19910418	JP 1989-511063	19891012
JP 2782693	B2	19980806		
AU 625683	B2	19920716	AU 1989-44228	19891012
CA 2000697	AA	19900414	CA 1989-2000697	19891013
US 5139790	A	19920818	US 1991-677573	19910329
US 5244668	A	19930914	US 1992-930325	19920817
PRIORITY APPLN. INFO.:			US 1988-257569	A2 19881014
			US 1988-264747	A 19881031
			WO 1989-US4533	W 19891012
			US 1991-677573	A3 19910329

IT Pharmaceutical dosage forms  
(tablets, buccal, PEG-contg. excipient for)  
IT 50-28-2, Estradiol, biological studies 54-11-5, Nicotine 58-18-4,  
Methyl testosterone  
RL: BIOL (Biological study)  
(buccal tablets contg., PEG-contg. excipient for)

L26 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1992:557675 CAPLUS  
DOCUMENT NUMBER: 117:157675  
TITLE: A buccal dosage form matrix containing polyethylene glycol  
INVENTOR(S): Snipes, Wallace C.  
PATENT ASSIGNEE(S): Zetachron, Inc., USA  
SOURCE: U.S., 6 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5135752	A	19920804	US 1988-257569	19881014
US 5004601	A	19910402	US 1988-264747	19881031
EP 390911	A1	19901010	EP 1989-911956	19891012
EP 390911	B1	19950301		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE			
JP 03501737	T2	19910418	JP 1989-511063	19891012
JP 2782693	B2	19980806		
AU 625683	B2	19920716	AU 1989-44228	19891012
CA 2000697	AA	19900414	CA 1989-2000697	19891013
US 5139790	A	19920818	US 1991-677573	19910329
US 5244668	A	19930914	US 1992-930325	19920817
PRIORITY APPLN. INFO.:			US 1988-257569	A2 19881014
			US 1988-264747	A 19881031
			WO 1989-US4533	W 19891012
			US 1991-677573	A3 19910329

- IT Pharmaceutical dosage forms  
(tablets, buccal, matrix for, polyoxyethylene and  
carboxylate and silica in)  
IT 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17.beta.)-, biological studies  
54-11-5, Nicotine 58-18-4, Methyl testosterone  
RL: BIOL (Biological study)

L2 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4  
ACCESSION NUMBER: 1996:8351 CAPLUS  
DOCUMENT NUMBER: 124:76746  
TITLE: Pharmacokinetics of a single dose of Buccal testosterone  
AUTHOR(S): Kim, Seokjoong; Snipes, Wallace; Hodgen, Gary D.; Anderson, Freedolph  
CORPORATE SOURCE: Jones Institute Reproductive Medicine, Eastern Virginia Medical School, Norfolk, VA, 23507, USA  
SOURCE: Contraception (1995), 52(5), 313-16  
CODEN: CCPTAY; ISSN: 0010-7824  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The bioavailability, pharmacokinetics, and metab. of a novel transbuccal delivery system of **testosterone** was investigated in five healthy eugonadal men. Total serum **testosterone** (T), dihydrotestosterone (DHT), and sex hormone-binding globulin (SHBG) concns. were detd. from blood samples obtained at 8:00 a.m. (zero hour), and 30 min and 1, 2, 3, 4, 6, 12 and 24 h later on day 1, and again on day 2, after dosing. This single transbuccal **administration** of **Buccal T** induced a prompt rise in serum T and DHT concns. The maximal concn. (Cmax) of T was 19.56 7.64 ng/mL (mean; 5.3-fold increase from the baseline) at 30 min (Tmax) after administration. The elimination half-life of Buccal T was about 1.75 h. Serum DHT peaked at 1 h at a concn. of 1.46 ng/mL (2.3-fold increase from the baseline). The drug was well tolerated. This study suggests that the Buccal T is a promising delivery system for natural T.

L2 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2002 ACS

DUPPLICATE 5

ACCESSION NUMBER: 1986:193013 CAPLUS

DOCUMENT NUMBER: 104:193013

TITLE: Hydrophilic cyclodextrin derivatives enable effective oral administration of steroid hormones

AUTHOR(S): Pitha, Josef; Harman, S. Mitchell; Michel, Mary Ellen

CORPORATE SOURCE: Natl. Inst. Aging, Baltimore, MD, 21224, USA

SOURCE: J. Pharm. Sci. (1986), 75(2), 165-7

CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Condensation products of .beta.-cyclodextrin with propylene oxide or epichlorohydrin, which are amorphous and thus very sol. in water, were used to form complexes with **testosterone** [58-22-0], progesterone [57-83-0], and estradiol [50-28-2]. Sublingual/**buccal administration** of tablets of these complexes led to effective absorption and entry of the hormones into the systemic circulation, followed by gradual elimination; rapid first-pass loss was avoided. .beta.-Cyclodextrin itself, its 2,6-di-Me deriv., and a nonionic detergent did not enable effective buccal absorption. Absorption from the GI tract of hormones complexed with hydrophilic cyclodextrins was also less effective. Effective absorption of drugs from the oral cavity requires that the drug and solubilizer form a complex of the inclusion type which dissolves completely and rapidly and that the solubilizer neither enters nor damages oral tissue.

ANSWER 13 OF 13 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1985:32254 CAPLUS  
DOCUMENT NUMBER: 102:32254  
TITLE: Administration of sex hormones in the form of  
hydrophilic cyclodextrin derivatives  
INVENTOR(S): Pitha, Josef  
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA  
SOURCE: U. S. Pat. Appl., 20 pp. Avail. NTIS Order No.  
PAT-APPL-6-603 839.  
CODEN: XAXXAV  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
US 603839	A0	19840831	US 1984-603839	19840425
US 4596795	A	19860624		
US 4727064	A	19880223	US 1985-738749	19850529

PRIORITY APPLN. INFO.: US 1984-603839 19840425

AB Sex hormones such as estradiol, progesterone, and **testosterone** administered as cyclodextrin deriv. inclusion compds. by sublingual or **buccal route** results in their effective transfer into the systemic circulation followed by only gradual elimination. The compds. are active only by this route and not from the gastrointestinal tract due to fast metab. of hormones by liver. Thus, a **testosterone** compd. with hydroxypropyl .beta.-cyclodextrin (hormone, 10 mg) tablet administered sublingually to a caucasian male with a hypopituitary condition showed a hormone level of 1020 ng/100 mL serum at 2 h after administration compared to 480 ng from a gelatin capsule.

L8: Entry 8 of 11

File: JPAB

Apr 27, 1989

PUB-N0: JP401110622A

DOCUMENT-IDENTIFIER: JP 01110622 A

TITLE: INTERMITTENTLY-RELEASING PREPARATION FOR APPLYING TO ORAL CAVITY

PUBN-DATE: April 27, 1989

## INVENTOR-INFORMATION:

NAME	COUNTRY
WATOU, TAKAHIKO	
HAMA, TERUO	
INOUE, NOBUKO	
TADA, YUKIHIRO	
HISAICHI, SHINICHI	

## ASSIGNEE-INFORMATION:

NAME	COUNTRY
TEIKOKU SEIYAKU KK	

APPL-NO: JP62267221

APPL-DATE: October 21, 1987

INT-CL (IPC): A61K 9/70

## ABSTRACT:

PURPOSE: To obtain a preparation for oral cavity, by allowing the release-controlling layer to include the drug-containing layer, thus the resultant preparation can be orally given, control the drug release intermittently, and reduce the releasing time and administration frequency.

CONSTITUTION: The subject preparation is produced by allowing the release-controlling layer which is mainly composed of a water-soluble or water-swelling polymer such as cellulose derivative or polyacrylic acid to include another layer containing 1 or more than 2 drugs, and laminating the release-controlling layers and the drug-containing layers, and tabletting the laminated product in a usual manner. The product is formulated into a drug for oral cavity, such as buccal tablets, troche, sublingual tablets or the like. It can avoid the influence of pH in digestive tracts by oral administration whereby the active ingredients are stably released. The problems of chronic toxicity caused by persistency and drug resistance also can be resolved.

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L8: Entry 8 of 11

File: JPAB

Apr 27, 1989

PUB-N0: JP401110622A

DOCUMENT-IDENTIFIER: JP 01110622 A

TITLE: INTERMITTENTLY-RELEASING PREPARATION FOR APPLYING TO ORAL CAVITY

PUBN-DATE: April 27, 1989

## INVENTOR-INFORMATION:

NAME	COUNTRY
WATOU, TAKAHIKO	
HAMA, TERUO	
INOUE, NOBUKO	
TADA, YUKIHIRO	
HISAICHI, SHINICHI	

## ASSIGNEE-INFORMATION:

NAME	COUNTRY
TEIKOKU SEIYAKU KK	

APPL-NO: JP62267221

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INT-CL (IPC): A61K 9/70

## ABSTRACT:

PURPOSE: To obtain a preparation for oral cavity, by allowing the release-controlling layer to include the drug-containing layer, thus the resultant preparation can be orally given, control the drug release intermittently, and reduce the releasing time and administration frequency.

CONSTITUTION: The subject preparation is produced by allowing the release-controlling layer which is mainly composed of a water-soluble or water-swelling polymer such as cellulose derivative or polyacrylic acid to include another layer containing 1 or more than 2 drugs, and laminating the release-controlling layers and the drug-containing layers, and tableting the laminated product in a usual manner. The product is formulated into a drug for oral cavity, such as buccal tablets, troche, sublingual tablets or the like. It can avoid the influence of pH in digestive tracts by oral administration whereby the active ingredients are stably released. The problems of chronic toxicity caused by persistency and drug resistance also can be resolved.

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